IRAC MoA Classification Scheme

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1. Introduction

The IRAC Mode of Action (MoA) classification provides growers, advisors, extension staff, consultants and crop protection professionals with a guide to the selection of insecticides or acaricides for use in an effective and sustainable insecticide or acaricide resistance management (IRM) strategy. In addition to presenting the MoA classification, this document outlines the background to, and purposes of, the classification list, and provides guidance on how it is used for IRM purposes. The list is reviewed and re-issued at intervals, as required.

2. What is resistance?

Resistance to insecticides may be defined as '*a heritable change in the sensitivity of a pest population that is reflected in the repeated failure of a product to achieve the expected level of control when used according to the label recommendation for that pest species*' (IRAC). This definition differs slightly from others in the literature, but IRAC believes it represents the most accurate practical definition of relevance to growers. Resistance arises through the over-use or misuse of an insecticide or acaricide against a pest species and results from the selection of resistant forms of the pest and the consequent evolution of populations that are resistant to that insecticide or acaricide.

3. MoA, Target-site resistance and Cross-resistance

In the majority of cases, not only does resistance render the selecting compound ineffective but it often also confers cross-resistance to other chemically related compounds. This is because compounds within a specific chemical group usually share a common target site within the pest, and thus share a common MoA. It is common for resistance to develop that is based on a genetic modification of this target site. When this happens, the interaction of the selecting compound with its target site is impaired and the compound loses its pesticidal efficacy. Because all compounds within the chemical sub-group share a common MoA, there is a high risk that the resistance that has developed will automatically confer cross-resistance to all compounds in the same sub-group. It is this concept of cross-resistance within a family of chemically related insecticides or acaricides that is the basis of the IRAC MoA classification.

4. Use of alternations or sequences of different MoAs

The objective of successful Insecticide Resistance Management (IRM) is to prevent or delay the evolution of resistance to insecticides, or to help regain susceptibility in insect pest populations in which resistance has already arisen. Effective IRM is thus an important element in maintaining the efficacy of valuable insecticides. It is important to recognize that it is usually easier to proactively prevent resistance from occurring than it is to reactively regain susceptibility. Nevertheless, the IRAC MoA classification will always provide valuable guidance to the design of effective IRM strategies.

Experience has shown that all effective insecticide or acaricide resistance management strategies seek to minimise the selection for resistance from any one type of insecticide or acaricide. In practice, alternations, sequences or rotations of compounds from different MoA groups provide a sustainable and effective approach to IRM. This ensures that selection from compounds in any one MoA group is minimised. The IRAC classification in this document is provided as an aid to insecticide selection for these types of IRM strategies.
Applications are often arranged into MoA spray windows or blocks that are defined by the stage of crop development and the biology of the pest(s) of concern. Local expert advice should always be followed with regard to spray windows and timings. Several sprays of a compound may be possible within each spray window, but successive generations of the pest should not be treated with compounds from the same MoA group.

5. Non-target site resistance mechanisms

It is fully recognized that resistance of insects and mites to insecticides and acaricides can, and frequently does, result from enhanced metabolism by enzymes within the pest. Such metabolic resistance mechanisms are not linked to any specific site of action classification and therefore they may confer resistance to insecticides in more than one IRAC MoA group. Where such metabolic resistance has been characterized and the cross-resistance spectrum is known, it is possible that certain alternations, sequences or rotations of MoA groups cannot be used. Similarly, mechanisms of reduced penetration of the pesticide into the pest, or behavioural changes of the pest may also confer resistance to multiple MoA groups. Where such mechanisms are known to give cross-resistance between MoA groups, the use of insecticides should be modified appropriately.

Where the resistance mechanism(s) is unknown, the intelligent use of alternations, sequences or rotations of compounds from different MoA classes remains an entirely viable resistance management technique, since such a practice will always minimise selection pressures.

6. The MoA Classification Scheme

The MOA classification scheme developed and endorsed by IRAC is based on the best available evidence of the MoA of available insecticides. Details of the listing have been agreed by IRAC companies and approved by internationally recognized industrial and academic insect toxicologists and biochemists.

It is our aim to ensure that insecticide and acaricide users are aware of MoA groups and that they have a sound basis on which to implement season-long, sustainable resistance management through the effective use of alternations, sequences or rotations of insecticides with different modes of action. To help delay resistance, it is strongly recommended that growers also integrate other control methods into insect or mite control programmes. Further advice is given in Appendix 2.

Note: Inclusion of a compound in the MoA list does not necessarily signify regulatory approval.

6.1. Rules for inclusion of a compound in the MoA list

- Chemical nomenclature is based on that appearing in *The Pesticide Manual*, 15th edition, November 2009, Ed. C.D.S. Tomlin, published by The British Crop Protection Council. ISBN 9781901396188
- To be included in the active list, compounds must have, or be very close to having, a minimum of one registered use in at least one country.
- In any one MoA classification sub-group, where more than one active ingredient in that chemical sub-group is registered for use, the chemical sub-group name is used.
- In any one MoA classification sub-group, where only one active ingredient is registered for use, the name of that exemplifying active ingredient is used
- Where more than one chemical sub-group or exemplifying active ingredient appears in a single MoA group, each is named according to the above rules, with chemical sub-groups having precedence over single active ingredients.

6.2. Classification Table

IRAC MoA Classification v 7.2, February 2012[1]		
Main Group and Primary Site of Action	**Chemical Sub-group or exemplifying Active Ingredient**	**Active Ingredients**
1* **Acetylcholinesterase (AChE) inhibitors** Nerve action {Strong evidence that action at this protein is responsible for insecticidal effects} ** Please see footnotes for further information on the use of compounds between sub-groups*	**1A** Carbamates	Alanycarb, Aldicarb, Bendiocarb, Benfuracarb, Butocarboxim, Butoxycarboxim, Carbaryl, Carbofuran, Carbosulfan, Ethiofencarb, Fenobucarb, Formetanate, Furathiocarb, Isoprocarb, Methiocarb, Methomyl, Metolcarb, Oxamyl, Pirimicarb, Propoxur, Thiodicarb, Thiofanox, Triazamate,Trimethacarb, XMC, Xylylcarb
	1B Organophosphates	Acephate, Azamethiphos, Azinphos-ethyl, Azinphos-methyl, Cadusafos, Chlorethoxyfos, Chlorfenvinphos, Chlormephos, Chlorpyrifos, Chlorpyrifos-methyl, Coumaphos, Cyanophos, Demeton-S-methyl, Diazinon, Dichlorvos/ DDVP, Dicrotophos, Dimethoate, Dimethylvinphos, Disulfoton, EPN, Ethion, Ethoprophos, Famphur, Fenamiphos, Fenitrothion, Fenthion, Fosthiazate, Heptenophos, Imicyafos, Isofenphos, Isopropyl *O*-(methoxyaminothio-phosphoryl) salicylate, Isoxathion, Malathion, Mecarbam, Methamidophos, Methidathion, Mevinphos, Monocrotophos, Naled, Omethoate, Oxydemeton-methyl, Parathion, Parathion-methyl, Phenthoate, Phorate, Phosalone, Phosmet, Phosphamidon, Phoxim, Pirimiphos- methyl, Profenofos, Propetamphos, Prothiofos, Pyraclofos, Pyridaphenthion, Quinalphos, Sulfotep, Tebupirimfos, Temephos, Terbufos, Tetrachlorvinphos, Thiometon, Triazophos, Trichlorfon, Vamidothion
2 **GABA-gated chloride channel antagonists** Nerve action {Strong evidence that action at this protein is responsible for insecticidal effects}	**2A** Cyclodiene organochlorines	Chlordane, Endosulfan
	2B Phenylpyrazoles (Fiproles)	Ethiprole, Fipronil
3* **Sodium channel modulators** Nerve action {Strong evidence that action at this protein is responsible for insecticidal effects} ** Please see footnotes for further information on the use of compounds between sub-groups*	**3A** Pyrethroids Pyrethrins	Acrinathrin, Allethrin, d-*cis-trans* Allethrin, d-*trans* Allethrin, Bifenthrin, Bioallethrin, Bioallethrin S-cyclopentenyl isomer , Bioresmethrin, Cycloprothrin, Cyfluthrin, *beta*-Cyfluthrin, Cyhalothrin, *lambda*-Cyhalothrin, *gamma*-Cyhalothrin, Cypermethrin, *alpha*-Cypermethrin, *beta*-Cypermethrin, *theta*-cypermethrin, *zeta*-Cypermethrin, Cyphenothrin , (1*R*)-*trans*- isomers], Deltamethrin, Empenthrin (*EZ*)- (1*R*)-isomers], Esfenvalerate, Etofenprox, Fenpropathrin, Fenvalerate, Flucythrinate, Flumethrin, *tau*-Fluvalinate, Halfenprox, Imiprothrin, Kadethrin, Permethrin, Phenothrin [(1*R*)-*trans*- isomer], Prallethrin, Pyrethrins (pyrethrum), Resmethrin, Silafluofen, Tefluthrin, Tetramethrin, Tetramethrin [(1*R*)-isomers], Tralomethrin, Transfluthrin,
	3B DDT Methoxychlor	DDT Methoxychlor

IRAC MoA Classification v 7.2, February 2012[1]		
Main Group and Primary Site of Action	**Chemical Sub-group or exemplifying Active Ingredient**	**Active Ingredients**
4 **Nicotinic acetylcholine receptor (nAChR) agonists** Nerve action {Strong evidence that action at one or more of this class of protein is responsible for insecticidal effects}	**4A** Neonicotinoids	Acetamiprid, Clothianidin, Dinotefuran, Imidacloprid, Nitenpyram, Thiacloprid, Thiamethoxam,
	4B Nicotine	Nicotine
	4C Sulfoxaflor	Sulfoxaflor
5 **Nicotinic acetylcholine receptor (nAChR) allosteric activators** Nerve action {Strong evidence that action at one or more of this class of protein is responsible for insecticidal effects}	Spinosyns	Spinetoram, Spinosad
6 **Chloride channel activators** Nerve and muscle action {Strong evidence that action at one or more of this class of protein is responsible for insecticidal effects}	Avermectins, Milbemycins	Abamectin, Emamectin benzoate, Lepimectin, Milbemectin
7 **Juvenile hormone mimics** Growth regulation {Target protein responsible for biological activity is unknown, or uncharacterized}	**7A** Juvenile hormone analogues	Hydroprene, Kinoprene, Methoprene
	7B Fenoxycarb	Fenoxycarb
	7C Pyriproxyfen	Pyriproxyfen
8 **Miscellaneous non-specific (multi-site) inhibitors**	**8A** Alkyl halides	Methyl bromide and other alkyl halides
	8B Chloropicrin	Chloropicrin
	8C Sulfuryl fluoride	Sulfuryl fluoride
	8D Borax	Borax
	8E Tartar emetic	Tartar emetic

IRAC MoA Classification v 7.2, February 2012[1]

Main Group and Primary Site of Action	Chemical Sub-group or exemplifying Active Ingredient	Active Ingredients
9 **Selective homopteran feeding blockers** Nerve action {Target protein responsible for biological activity is unknown, or uncharacterized}	**9B** Pymetrozine	Pymetrozine
	9C Flonicamid	Flonicamid
10 **Mite growth inhibitors** Growth regulation {Target protein responsible for biological activity is unknown, or uncharacterized}	**10A*** Clofentezine Hexythiazox Diflovidazin **Please see footnotes for further information on this sub-grouping*	Clofentezine, Hexythiazox, Diflovidazin
	10B Etoxazole	Etoxazole
11 **Microbial disruptors of insect midgut membranes** (includes transgenic crops expressing *Bacillus thuringiensis* toxins, however specific guidance for resistance management of transgenic crops is not based on rotation of modes of action)	**11A*** *Bacillus thuringiensis* and the insecticidal proteins they produce **Please see footnotes for further information on this sub-grouping*	*Bacillus thuringiensis* subsp. *israelensis* *Bacillus thuringiensis* subsp. *aizawai* *Bacillus thuringiensis* subsp. *kurstaki* *Bacillus thuringiensis* subsp. *tenebrionis* *B.t.* crop proteins: (* Please see footnote) Cry1Ab, Cry1Ac, Cry1Fa, Cry1A.105, Cry2Ab, Vip3A, mCry3A, Cry3Ab, Cry3Bb, Cry34Ab1/Cry35Ab1
	11B *Bacillus sphaericus*	*Bacillus sphaericus*
12 **Inhibitors of mitochondrial ATP synthase** Energy metabolism {Compounds affect the function of this protein, but it is not clear that this is what leads to biological activity}	**12A** Diafenthiuron	Diafenthiuron
	12B Organotin miticides	Azocyclotin, Cyhexatin, Fenbutatin oxide
	12C Propargite	Propargite
	12D Tetradifon	Tetradifon
13 **Uncouplers of oxidative phosphorylation via disruption of the proton gradient** Energy metabolism	Chlorfenapyr DNOC Sulfluramid	Chlorfenapyr DNOC Sulfluramid

IRAC MoA Classification v 7.2, February 2012[1]		
Main Group and Primary Site of Action	**Chemical Sub-group or exemplifying Active Ingredient**	**Active Ingredients**
14 **Nicotinic acetylcholine receptor (nAChR) channel blockers** Nerve action {Compounds affect the function of this protein, but it is not clear that this is what leads to biological activity}	Nereistoxin analogues	Bensultap, Cartap hydrochloride, Thiocyclam, Thiosultap-sodium
15 **Inhibitors of chitin biosynthesis, type 0** Growth regulation {Target protein responsible for biological activity is unknown, or uncharacterized}	Benzoylureas	Bistrifluron, Chlorfluazuron, Diflubenzuron, Flucycloxuron, Flufenoxuron, Hexaflumuron, Lufenuron, Novaluron, Noviflumuron, Teflubenzuron, Triflumuron
16 **Inhibitors of chitin biosynthesis, type 1** Growth regulation {Target protein responsible for biological activity is unknown, or uncharacterized}	Buprofezin	Buprofezin
17 **Moulting disruptor, Dipteran** Growth regulation {Target protein responsible for biological activity is unknown, or uncharacterized}	Cyromazine	Cyromazine
18 **Ecdysone receptor agonists** Growth regulation {Strong evidence that action at this protein is responsible for insecticidal effects}	Diacylhydrazines	Chromafenozide, Halofenozide, Methoxyfenozide, Tebufenozide

IRAC MoA Classification v 7.2, February 2012[1]		
Main Group and Primary Site of Action	**Chemical Sub-group or exemplifying Active Ingredient**	**Active Ingredients**
19 **Octopamine receptor agonists** Nerve action {Good evidence that action at one or more of this class of protein is responsible for insecticidal effects}	Amitraz	Amitraz
20 **Mitochondrial complex III electron transport inhibitors** Energy metabolism {Good evidence that action at this protein complex is responsible for insecticidal effects}	**20A** Hydramethylnon	Hydramethylnon
	20B Acequinocyl	Acequinocyl
	20C Fluacrypyrim	Fluacrypyrim
21 **Mitochondrial complex I electron transport inhibitors** Energy metabolism {Good evidence that action at this protein complex is responsible for insecticidal effects}	**21A** METI acaricides and insecticides	Fenazaquin, Fenpyroximate, Pyrimidifen, Pyridaben, Tebufenpyrad, Tolfenpyrad
	21B Rotenone	Rotenone (Derris)
22* **Voltage-dependent sodium channel blockers** Nerve action {Good evidence that action at this protein complex is responsible for insecticidal effects} **Please see footnotes for further information on sub-grouping*	**22A** Indoxacarb	Indoxacarb
	22B Metaflumizone	Metaflumizone
23 **Inhibitors of acetyl CoA carboxylase.** Lipid synthesis, growth regulation {Good evidence that action at this protein is responsible for insecticidal effects}	Tetronic and Tetramic acid derivatives	Spirodiclofen, Spiromesifen, Spirotetramat

IRAC MoA Classification v 7.2, February 2012[1]		
Main Group and Primary Site of Action	**Chemical Sub-group or exemplifying Active Ingredient**	**Active Ingredients**
24 **Mitochondrial complex IV electron transport inhibitors** Energy metabolism {Good evidence that action at this protein complex is responsible for insecticidal effects}	**24A** Phosphine	Aluminium phosphide, Calcium phosphide, Phosphine, Zinc phosphide
	24B Cyanide	Cyanide
25 **Mitochondrial complex II electron transport inhibitors** Energy metabolism {Good evidence that action at this protein complex is responsible for insecticidal effects}	Beta-ketonitrile derivatives	Cyenopyrafen, Cyflumetofen
28 **Ryanodine receptor modulators** Nerve and muscle action {Good evidence that action at this protein complex is responsible for insecticidal effects}	Diamides	Chlorantraniliprole, Cyantraniliprole, Flubendiamide
un **Compounds of unknown or uncertain MoA[2]** {Target protein responsible for biological activity is unknown, or uncharacterized}	Azadirachtin	Azadirachtin
	Benzoximate	Benzoximate
	Bifenazate	Bifenazate
	Bromopropylate	Bromopropylate
	Chinomethionat	Chinomethionat
	Cryolite	Cryolite
	Dicofol	Dicofol
	Pyridalyl	Pyridalyl
	Pyrifluquinazon	Pyrifluquinazon

Table Notes:
MoA assignments will usually involve identification of the target protein responsible for the biological effect, although groupings can be made where compounds share distinctive physiological effects and have related chemical structures.
Groups 26 and 27 are unassigned at this time and have therefore been omitted from the table.

[1] Inclusion of a compound in the classification above does not necessarily signify regulatory approval
[2] A compound with an unknown or controversial MoA or an unknown mode of toxicity will be held in category 'un' until evidence becomes available to enable that compound to be assigned to a more appropriate MoA class

6.3. Criteria for descriptors of the quality of MoA information

{Strong evidence that action at this protein (or protein complex) is responsible for insecticidal effects}	Potent effects on the function of the target protein and either resistance due to mutation / overexpression / removal of this protein or correlation of potency between effects on the protein and biological activity for a set of analogues.
{Good evidence that action at this protein (or protein complex) is responsible for insecticidal effects}	Highly potent effects on the function of the protein combined with clearly consistent physiological effects
{Compounds affect the function of this protein, but it is not clear that this is what leads to biological activity}	Compounds (or their metabolites) have moderate or low potency on the function of the protein, and there is little or no evidence associating this effect with biological activity. Compounds may be grouped because of similarity of structure and distinctive physiological effect.
{Target protein responsible for biological activity is unknown, or uncharacterized}	Compounds may be grouped because of similarity of structure and distinctive physiological effect.

6.4. Notes regarding sub-groups

In the absence of other alternatives, it may be possible to rotate compounds between sub-groups if it is clear that cross resistance mechanisms do not exist in the target populations. By definition, subgroups are established to represent distinct chemical classes with a common MoA. Whether they should be rotated or not will depend on knowledge and experience of cross-resistance patterns, resistance mechanisms, and furthermore on the pest, crop and region considered.

Sub-groups represent distinct structural classes believed to have the same MoA. In principle, they provide a useful level of differentiation between compounds that may bind at the same target site but are nevertheless structurally different enough that the risk of metabolic cross-resistance is lower than for close chemical analogs. Subgroups are likely to be metabolized by different enzymes and may bind differently enough within the target site that the chance of selection for either metabolic or target-site resistance is reduced compared to close analogs.

Sub-groups	Notes
1A & 1B	If there are no other alternatives, compounds from groups 1A and 1B may be rotated in situations where cross-resistance mechanisms are known to be absent in the insect populations to be treated.
3A & 3B	If there are no other alternatives, compounds from groups 3A and 3B may be rotated in situations where cross-resistance mechanisms (e.g., kdr) are known to be absent in the insect populations to be treated. Because DDT is no longer used in agriculture, this is only applicable for the control of human disease vectors such as mosquitoes, because of a lack of alternatives.
4A, 4B & 4C	Although these compounds are believed to have the same target site, current evidence indicates that the risk of metabolic cross-resistance between groups 4A and 4C is low. If there are no other alternatives, compounds from groups 4A and 4C may be rotated in situations where cross-resistance mechanisms are known to be absent in the insect populations to be treated.
10A	Hexythiazox is grouped with clofentezine because they commonly exhibit cross-resistance, even though they are structurally distinct, and the target site for neither compound is known. Diflovidazin has been added to this group because it is a close analogue of Clofentezine and expected to have the same mode of action.
11A	Different *Bacillus thuringiensis* products that target different insect orders may be used together without compromising their resistance management. Rotation between certain specific Bacillus thuringiensis microbial products may provide resistance management benefits for some pests. Consult product-specific recommendations. *B.t.* Crop Proteins: Where there are differences among the specific receptors within the midguts of target insects, transgenic crops containing certain combinations of the listed proteins provide resistance management benefits.
22A & 22B	Although these compounds are believed to have the same target site, they have been sub-grouped because they are chemically distinct, and current evidence indicates that the risk of metabolic cross-resistance is low.

6.5. General notes & MoA Classification Scheme Updates

- Further details on the MoA Group Descriptors are given in Appendix 3.
- A list of active ingredients in alphabetical order with their respective MoA classification is given in Appendix 5.
- The Classification Scheme has been prepared using the most up-to-date information available to IRAC. It is provided to user groups, grower organisations, extension personnel, regulatory authorities such as the US EPA and all those involved in resistance management, as an agreed definitive statement by the agrochemical industry on the MoA of insecticides currently in use.
- The IRAC MoA classification is reviewed and reissued at intervals as required. The latest version is always available for reference via the IRAC website (www.irac-online.org).
- Submissions for new active ingredients together with recommendations for their inclusion in specific new or existing MoA classes, together with citations or evidence for classification should be made to IRAC through the website.
- IRAC member companies review draft versions before an agreed final version of any update is published. In addition, a number of internationally well-known insect toxicologists and biochemists can be consulted regarding additions, deletions or other changes to the list. Details of the procedures followed for allocation of new insecticidal materials to the MoA classification are given in Appendix 4.
- Changes to the listing may have serious consequences. In those countries where insecticide labels display the IRAC MoA number or class name as an aid to good IRM (see Appendix 1), changes may be especially costly to implement. In general, changes are therefore only endorsed when the scientific evidence supporting the change is compelling.
- Superseded, obsolete or withdrawn compounds for which no current registration exists, and that are no longer in common usage, are not listed.
- In a continued effort to refine the list, readers are kindly asked to inform IRAC of factual errors or omissions, citing definitive evidence wherever possible. Such submissions should be directed to IRAC via the website. Suggestions for improvements are likewise welcome.

Appendix 1

Product labels: Indication of MoA of active ingredient and accompanying IRM advice

To assist users in the selection of insecticides for use in IRM strategies employing sequences, rotations or alternations of MoA groups, IRAC is encouraging producers to clearly indicate the IRAC MoA group number and description on the product label, and to accompany this with appropriate advice of the type indicated below. Thus, in addition to the detailed product information, handling, and safety information required by local regulations, a typical title label should clearly indicate the IRAC MoA Group number & description, and minimal, brief advice on IRM as indicated in the example below.

example

Insecticide ® 50 SC

IRAC MoA Group 15
Inhibitors of chitin biosynthesis, type 0
Benzoylureas

Active Ingredient: [Compound name]
Formulation details

For resistance management purposes, Insecticide 50SC is an IRAC MoA Group 15 insecticide. Any insect population may contain individuals naturally resistant to Insecticide 50SC and other Group 15 insecticides. If these insecticides are used repeatedly, the resistant individuals may eventually dominate the pest insect population. These resistant insects may not be controlled by Insecticide 50SC or by other Group 15 insecticides. To delay the development of resistance:

- Avoid exclusive repeated use of insecticides from the same chemical subgroup, (indicated by the IRAC MoA Group number).
- Alternate with products from other IRAC MoA Groups
- Integrate other control methods (chemical, cultural, biological) into insect control programs.

For further information on resistance management and advice on IRM programmes contact your local distributor.

Appendix 2

IRM principles recommended and endorsed by IRAC

- Consult a local agricultural advisor or extension services in the area for up-to-date recommendations and advice on IPM and IRM programmes.
- Consider options for minimizing insecticide use by selecting early-maturing or pest-tolerant varieties of crop plants.
- Include effective cultural and biological control practices that work in harmony with effective IRM programmes. Adopt all non-chemical techniques known to control or suppress pest populations, including biological sprays such as Bt's, resistant varieties, within-field refugia (untreated areas) and crop rotation.
- Where possible select insecticides and other pest management tools, which preserve beneficial insects.
- Use products at their full, recommended doses. Reduced (sub-lethal) doses quickly select populations with average levels of tolerance, whilst doses that are too high may impose excessive selection pressures.
- Appropriate, well-maintained equipment should be used to apply insecticides. Recommended water volumes, spray pressures and optimal temperatures should be used to obtain optimal coverage.
- Where larval stages are being controlled, target younger larval instars where possible because these are usually much more susceptible and therefore much more effectively controlled by insecticides than older stages.
- Use appropriate local economic thresholds and spray intervals.
- Follow label recommendations or local expert advice for use of alternations or sequences of different classes of insecticide with differing modes of action as part of an IRM strategy.
- Where there are multiple applications per year or growing season, alternate products of different MoA classes.
- In the event of a control failure, do not reapply the same insecticide but change the class of insecticides to one having a different MoA and to which there is no [locally] known cross-resistance.
- Mixtures may offer a short-term solution to resistance problems, but it is essential to ensure that each component of a mixture belongs to a different insecticide MoA class, and that each component is used at its full rate.
- Consideration should be given to monitoring for the incidence of resistance in the most commercially important situations and gauge levels of control obtained.
- Withholding use of a product to which resistance has developed until susceptibility returns may be a valid tactic if sufficient alternative chemical classes remain to provide effective control.

Appendix 3

MoA Group Descriptors

Nerve and Muscle Targets

Most current insecticides act on nerve and muscle targets. Insecticides that act on these targets are generally fast acting.

Group 1 Acetylcholinesterase (AChE) inhibitors
Inhibit AChE, causing hyperexcitation. AChE is the enzyme that terminates the action of the excitatory neurotransmitter acetylcholine at nerve synapses.

Group 2 GABA-gated chloride channel antagonists
Block the GABA-activated chloride channel, causing hyperexcitation and convulsions. GABA is the major inhibitory neurotransmitter in insects.

Group 3 Sodium channel modulators
Keep sodium channels open, causing hyperexcitation and, in some cases, nerve block. Sodium channels are involved in the propagation of action potentials along nerve axons.

Group 4 Nicotinic acetylcholine receptor (nAChR) agonists
Mimic the agonist action of acetylcholine at nAChRs, causing hyperexcitation. Acetylcholine is the major excitatory neurotransmitter in the insect central nervous system.

Group 5 Nicotinic acetylcholine receptor (nAChR) allosteric modulators
Allosterically activate nAChRs, causing hyperexcitation of the nervous system. Acetylcholine is the major excitatory neurotransmitter in the insect central nervous system.

Group 6 Chloride channel activators
Allosterically activate glutamate-gated chloride channels (GluCls), causing paralysis. Glutamate is an important inhibitory neurotransmitter in insect.

Group 9 Selective homopteran feeding blockers
Incompletely defined MoA causing selective inhibition of aphid and whitefly feeding.

Group 14 Nicotinic acetylcholine receptor (nAChR) channel blockers
Block the nAChR ion channel, resulting in nervous system block and paralysis. Acetylcholine is the major excitatory neurotransmitter in the insect central nervous system.

Group 19 Octopamine receptor agonists
Activate octopamine receptors, leading to hyperexcitation. Octopamine is the insect equivalent of adrenaline, the fight-or-flight neurohormone.

Group 22 Voltage-dependent sodium channel blockers
Block sodium channels, causing nervous system shutdown and paralysis.
Sodium channels are involved in the propagation of action potentials along nerve axons.

Group 28 Ryanodine receptor modulators
Activate muscle ryanodine receptors, leading to contraction and paralysis. Ryanodine receptors mediate calcium release into the cytoplasm from intracellular stores.

Growth and Development Targets

Insect development is controlled by the balance of two principal hormones: juvenile hormone and ecdysone. Insect growth regulators act by mimicking one of these hormones or directly perturbing cuticle formation/deposition or lipid biosynthesis. Insecticides that act on individual targets in this system are generally slow to moderately slow acting.

Group 7 Juvenile hormone mimics
Applied in the pre-metamorphic instar, these compounds disrupt and prevent metamorphosis.

Group 10 Mite growth inhibitors
Incompletely defined MoA leading to growth inhibition

Group 15 Inhibitors of chitin biosynthesis, type 0
Incompletely defined MoA leading to inhibition of chitin biosynthesis.

Group 16 Inhibitors of chitin biosynthesis, type 1
Incompletely defined MoA leading to inhibition of chitin biosynthesis in a number of insects, including whiteflies.

Group 17 Moulting disruptor, Dipteran
Incompletely defined MoA that leads to moult disruption.

Group 18 Ecdysone receptor agonists
Mimic the moulting hormone, ecdysone, inducing a precocious moult.

Group 23 Inhibitors of acetyl CoA carboxylase
Inhibit acetyl coenzyme A carboxylase, part of the first step in lipid biosynthesis, leading to insect death.

Respiration Targets

Mitochondrial respiration produces ATP, the molecule that energizes all vital cellular processes. In mitochondria, an electron transport chain stores the energy released by oxidation in the form of a proton gradient, which drives ATP synthesis. Several insecticides are known to interfere with mitochondrial respiration by the inhibition of electron transport and/or oxidative phosphorylation. Insecticides that act on individual targets in this system are generally fast to moderately fast acting.

Group 12 Inhibitors of mitochondrial ATP synthase
Inhibit the enzyme that synthesizes ATP.

Group 13 Uncouplers of oxidative phosphorylation via disruption of the proton gradient
Protonophores that short-circuit the mitochondrial proton gradient so that ATP can not be synthesized.

Group 20 Mitochondrial complex III electron transport inhibitors
Inhibit electron transport complex III, preventing the utilization of energy by cells.

Group 21 Mitochondrial complex I electron transport inhibitors
Inhibit electron transport complex I, preventing the utilization of energy by cells.

Group 24 Mitochondrial complex IV electron transport inhibitors
Inhibit electron transport complex IV, preventing the utilization of energy by cells.

Group 25 Mitochondrial complex II electron transport inhibitors
Inhibit electron transport complex II, preventing utilization of energy by cells.

Midgut Targets

Lepidopteran-specific microbial toxins that are sprayed or expressed in transgenic crop varieties.

Group 11 Microbial disruptors of insect midgut membranes
Protein toxins that bind to receptors on the midgut membrane and induce pore formation, resulting in ionic imbalance and septicemia.

Unknown or non-specific targets

Several insecticides are known to affect less well-described target-sites or functions, or to act non-specifically on multiple targets.

Group 8 Miscellaneous non-specific (multi-site) inhibitors

Appendix 4

Procedure for allocation of new insecticidal materials to the MoA classification

IRAC maintains the MoA Classification scheme as the definitive, globally-recognised, ultimate authority on insecticide modes of action. In order to provide the best possible information for resistance management purposes, IRAC also issues regular updates of the scheme, in which newly introduced insecticides are allocated to an appropriate MoA classification group and structural sub-group, and in which re-classification or the correction of errors or anomalies for specific compounds is undertaken in light of definitive new information. This document details how these processes are administered by IRAC.

Who is responsible for the process within IRAC?

The IRAC MoA Team comprises technical representatives of the member companies with expertise in insect toxicology, pharmacology or biochemistry. All IRAC companies are eligible to contribute technical expertise to the group. The group meets regularly to consider the content and detail of the MoA scheme and makes proposals on significant additions, deletions or reallocations of compounds within the scheme for consideration by the IRAC Executive.

Why and how often is the scheme updated?

New versions of the scheme are issued periodically as and when necessary, as a result of the MoA Team's consideration of new information. The introduction of major new MoA groups or the reallocation of compounds or groups would merit the issue of a new version (vN). Minor changes or corrections that do not significantly impact the scheme are undertaken automatically at intervals as necessary, and sub-versions are issued (vN.n). New sub-versions may be issued up to several times per year as required, while new full versions are not anticipated more than once per year. The potential impact of proposed significant changes on derived versions of the scheme around the world is fully appreciated, especially in countries where MoA labelling of products is used. The MoA team is cognisant of these impacts and revisions are only proposed when the evidence for change is scientifically compelling.

What evidence is needed to support MoA classification of a compound?

Proposals for additions to the MoA scheme or for amendments to the current scheme should be submitted to the IRAC MoA team (details below). These proposals will be considered by the Team and a decision on the outcome will be provided to the proposer in due course. Published material in high quality, front line, peer-reviewed, scientific journals is especially useful as a source of information for consideration by the team, and those companies, bodies or individuals submitting proposals for consideration by the team are strongly encouraged to provide such information wherever possible. Corroborating information is also especially welcome. Unpublished material may be submitted in evidence, and the MoA team will interpret this appropriately.

Several types of data can be used to establish MoA (including the activation of pro-insecticides to their actives). Convincing evidence to support the MoA hypothesis is needed. This includes the demonstration of a clear target effect (activation, inhibition, or modulation) at concentrations that can reasonably be expected in the intoxicated organism. Preferably, these data may be corroborated by physiological and/or symptomology studies to link insect mortality to the effect on the target site. A positive structure-activity correlation of *in vitro* efficacy with insecticidal potency, and/or target site mutations conferring resistance are required to further substantiate the proposed MoA.

What are the criteria for establishing MoA Subgroups?

Subgroups represent distinct chemical classes believed to have the same MoA, but that are different enough in chemical structure, or mode of interaction at the target protein, that the chance of selection for either metabolic or target-site cross-resistance is reduced compared to close analogs.

Subgroups may also distinguish compounds that may be chemically similar, but known to bind differently within the target or have differential selectivity among multiple targets. The cross-resistance potential between subgroups is higher than that between groups, and therefore rotation between subgroups should be avoided, except where there are no alternatives from other groups, and when cross-resistance mechanisms do not exist in the target populations.

How are decisions made by the MoA Team?

Given the definitive nature of the IRAC MoA scheme, the MoA Team regards it as an absolute priority that the highest levels of scientific integrity are always employed in the consideration and discussion of allocation of compounds. In general, agreement on allocation of a compound is usually arrived at through consensus within the Team following detailed discussion. Major decisions, for example the introduction of new MoA classes or sub-classes are proposed to the IRAC Executive for ratification. In the event that the Team cannot agree it may choose to place the case with a panel of external MoA experts to gain their written opinion before reconsidering the case. The composition of the expert panel is agreed in advance by the Team. If after reconsidering the particular case the team is still in disagreement, the matter will be passed to the IRAC Executive for further consideration. Where individual members of the Team are subject to a conflict of interests through company affiliation or other interests, they may choose to withdraw from discussion of particular compounds as they consider appropriate.

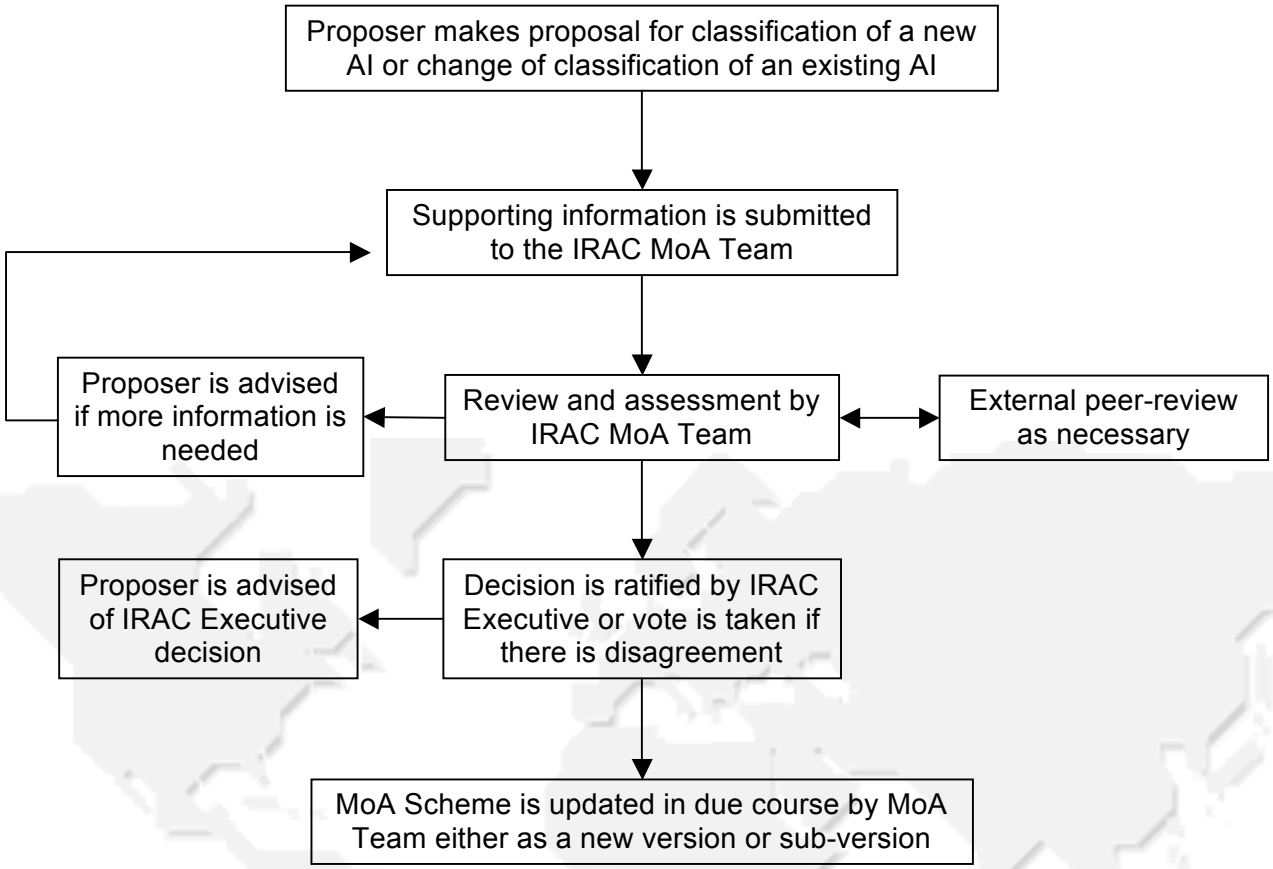
How long does this process take?

The MoA Team has a duty to make a definitive decision on allocation of a compound as quickly as possible following receipt of appropriate supporting evidence. For straightforward cases that do not require external consultation it should generally be expected that the Team could provide feedback to proposers within 3 months. The need for external consultants may extend the process to 6 months.

To whom should proposals be sent?

Proposals for new compounds or for changes to the current IRAC MoA scheme should be submitted to the IRAC MoA Team via the IRAC International Coordinator. A link to the coordinator is provided on the IRAC website (www.irac-online.org) at the bottom of each page under ‘Contact’.

Procedure for updates to IRAC MoA Classification Scheme



Appendix 5

Active Ingredients (Alphabetical Order) with MOA Classification

Active Ingredient	MOA No.
Abamectin	6
Acephate	1B
Acequinocyl	20B
Acetamiprid	4A
Acrinathrin	3A
Alanycarb	1A
Aldicarb	1A
Allethrin	3A
alpha-Cypermethrin	3A
Aluminium phosphide	24A
Amitraz	19
Azadirachtin	UN
Azamethiphos	1B
Azinphos-ethyl	1B
Azinphos-methyl	1B
Azocyclotin	12B
Bacillus thuringiensis	11A
Bacillus sphaericus	11B
Bendiocarb	1A
Benfuracarb	1A
Bensultap	14
Benzoximate	UN
beta-Cyfluthrin	3A
beta-Cypermethrin	3A
Bifenazate	UN
Bifenthrin	3A
Bioallethrin	3A
Bioallethrin S-cyclopentenyl isomer	3A
Bioresmethrin	3A
Bistrifluron	15
Borax	8D
Bromopropylate	UN
Buprofezin	16
Butocarboxim	1A
Butoxycarboxim	1A
Cadusafos	1B
Calcium phosphide	24A
Carbaryl	1A
Carbofuran	1A

Active Ingredient	MOA No.
Carbosulfan	1A
Cartap hydrochloride	14
Chinomethionat	UN
Chlorantraniliprole	28
Chlordane	2A
Chlorethoxyfos	1B
Chlorfenapyr	13
Chlorfenvinphos	1B
Chlorfluazuron	15
Chlormephos	1B
Chloropicrin	8B
Chlorpyrifos	1B
Chlorpyrifos-methyl	1B
Chromafenozide	18
Clofentezine	10A
Clothianidin	4A
Coumaphos	1B
Cryolite	UN
Cyanide	24B
Cyanophos	1B
Cyantraniliprole	28
Cycloprothrin	3A
Cyenopyrafen	25
Cyflumetofen	25
Cyfluthrin	3A
Cyhalothrin	3A
Cyhexatin	12B
Cypermethrin	3A
Cyphenothrin (1*R*)-*trans*-isomers]	3A
Cyromazine	17
d-*cis*-*trans* Allethrin	3A
DDT	3B
Deltamethrin	3A
Demeton-S-methyl	1B
Diafenthiuron	12A
Diazinon	1B
Dichlorvos/ DDVP	1B
Dicofol	UN
Dicrotophos	1B

Active Ingredient	MOA No.
Diflovidazin	10A
Diflubenzuron	15
Dimethoate	1B
Dimethylvinphos	1B
Dinotefuran	4A
Disulfoton	1B
DNOC	13
d-*trans* Allethrin	3A
Emamectin benzoate	6
Empenthrin [(EZ)-(1*R*)-isomers]	3A
Endosulfan	2A
EPN	1B
Esfenvalerate	3A
Ethiofencarb	1A
Ethion	1B
Ethiprole	2B
Ethoprophos	1B
Etofenprox	3A
Etoxazole	10B
Famphur	1B
Fenamiphos	1B
Fenazaquin	21A
Fenbutatin oxide	12B
Fenitrothion	1B
Fenobucarb	1A
Fenoxycarb	7B
Fenpropathrin	3A
Fenpyroximate	21A
Fenthion	1B
Fenvalerate	3A
Fipronil	2B
Flonicamid	9C
Fluacrypyrim	20C
Flubendimide	28
Flucycloxuron	15
Flucythrinate	3A
Flufenoxuron	15
Flumethrin	3A
Formetanate	1A
Fosthiazate	1B
Furathiocarb	1A
gamma-Cyhalothrin	3A
Halfenprox	3A

Active Ingredient	MOA No.
Halofenozide	18
Heptenophos	1B
Hexaflumuron	15
Hexythiazox	10A
Hydramethylnon	20A
Hydroprene	7A
Imicyafos	1B
Imidacloprid	4A
Imiprothrin	3A
Indoxacarb	22A
Isofenphos	1B
Isoprocarb	1A
Isopropyl O- (methoxyaminothio-phosphoryl) salicylate	1B
Isoxathion	1B
Kadethrin	3A
Kinoprene	7A
lambda-Cyhalothrin	3A
Lepimectin	6
Lufenuron	15
Malathion	1B
Mecarbam	1B
Metaflumizone	22B
Methamidophos	1B
Methidathion	1B
Methiocarb	1A
Methomyl	1A
Methoprene	7A
Methoxychlor	3B
Methoxyfenozide	18
Methyl bromide	8A
Metolcarb	1A
Mevinphos	1B
Milbemectin	6
Monocrotophos	1B
Naled	1B
Nicotine	4B
Nitenpyram	4A
Novaluron	15
Noviflumuron	15
Omethoate	1B
Oxamyl	1A
Oxydemeton-methyl	1B
Parathion	1B

Active Ingredient	MOA No.
Parathion-methyl	1B
Permethrin	3A
Phenothrin [(1*R*)- *trans*- isomer]	3A
Phenthoate	1B
Phorate	1B
Phosalone	1B
Phosmet	1B
Phosphamidon	1B
Phosphine	24A
Phoxim	1B
Pirimicarb	1A
Pirimiphos- methyl	1B
Prallethrin	3A
Profenofos	1B
Propargite	12C
Propetamphos	1B
Propoxur	1A
Prothiofos	1B
Pymetrozine	9B
Pyraclofos	1B
Pyrethrins (pyrethrum)	3A
Pyridaben	21A
Pyridalyl	UN
Pyridaphenthion	1B
Pyrifluquinazon	UN
Pyrimidifen	21A
Pyriproxyfen	7C
Quinalphos	1B
Resmethrin	3A
Rotenone (Derris)	21B
Silafluofen	3A
Spinetoram	5
Spinosad	5
Spirodiclofen	23
Spiromesifen	23
Spirotetramat	23
Sulfotep	1B

Active Ingredient	MOA No.
Sulfoxaflor	4C
Sulfuramid	13
Sulfuryl fluoride	8C
Tartar emetic	8E
tau-Fluvalinate	3A
Tebufenozide	18
Tebufenpyrad	21A
Tebupirimfos	1B
Teflubenzuron	15
Tefluthrin	3A
Temephos	1B
Terbufos	1B
Tetrachlorvinphos	1B
Tetradifon	12D
Tetramethrin	3A
Tetramethrin [(1*R*)- isomers]	3A
theta-cypermethrin	3A
Thiacloprid	4A
Thiamethoxam	4A
Thiocyclam	14
Thiodicarb	1A
Thiofanox	1A
Thiometon	1B
Thiosultap-sodium	14
Tolfenpyrad	21A
Tralomethrin	3A
Transfluthrin	3A
Triazamate	1A
Triazophos	1B
Trichlorfon	1B
Triflumuron	15
Trimethacarb	1A
Vamidothion	1B
XMC	1A
Xylylcarb	1A
zeta-Cypermethrin	3A
Zinc phosphide	24A